

## **REMARKS**

This Amendment is being submitted in response to the Office Action mailed on November 30, 2006 in connection with the above-identified application.

Reconsideration of the above-identified application in view of the following remarks is respectfully requested.

### **Status of Claims**

Claims 1-7, 9-21 and 23-33 are currently pending and under consideration. No amendments have been made to the currently pending claims.

### **Rejection of Claims 1-7, 9-21, and 23-33 Under 35 U.S.C. §103(a)**

The Office Action rejects claims 1-7, 9-21 and 23-33 under 35 U.S.C. §103(a) as being unpatentable over Phillips (U.S. Patent No. 6,489,346 B1) (hereinafter "Phillips I"). The Office further rejects claims 1-7, 9-21 and 23-33 under 35 U.S.C. §103(a) as being unpatentable over Phillips (U.S. Patent No. 5,840,737) (hereinafter "Phillips II") in view of Phillips I. Applicants respectfully traverse these rejections.

#### **a) Rejection of Claims 1-7, 9-21 and 23-33 over Phillips I**

The Examiner states that Phillips I teaches a method for treating acid-related gastrointestinal disorders comprising administering to a patient a non-enteric pharmaceutical composition comprising a non-enteric coated proton pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent, wherein the pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal (page 3 of Office Action). The Examiner further suggests that the Phillips I reference teaches that mixtures of the buffering agents can be used and such buffering agents include various bicarbonate and carbonate salts. More particularly, the Examiner states that the

sodium bicarbonate range in Phillips I is in the amounts about 1000mg to about 1680mg, which overlaps in range with the range recited in claim 9. Overall, the Examiner has maintained the exact same rejections based on Phillips as previously provided in prior rejections.

The Examiner has maintained the same rejections over Phillips I, even in view of the fact that the Examiner acknowledges that Phillips I does not teach an equimolar ratio of sodium bicarbonate and sodium carbonate. Nevertheless, the Examiner states that prior art teaches the use of the same drug and components in similar dosage forms as the instant invention. Applicant disagrees with the Examiner and believes that the present invention is distinguishable over the Phillips reference based on the unique buffering agent comprised of an equimolar ratio of bicarbonate salt and carbonate salt. Such equimolar ratio is not even contemplated nor obvious in view of Phillips I.

Phillips I does not either expressly or inherently teach the equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Similarly, Phillips I does not suggest or teach an equimolar ratio of sodium bicarbonate and sodium carbonate. Phillips I merely suggests that various combinations of salts may be used as a buffering agent, including bicarbonate salt and carbonate salt. Phillips I discloses a composition comprising a non-enteric coated proton pump inhibitor and at least one buffering agent. With respect to buffering agents, Phillips I states that the preferred buffering agent is sodium bicarbonate. (See, Phillips I, column 13, lines 33-40). Although the reference states broadly that “many other weak and strong bases (and mixtures thereof) can be utilized” and provides a non-exhaustive list of examples of buffering agents including sodium bicarbonate, potassium bicarbonate, magnesium hydroxide, etc., nowhere does Phillips I suggest an equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. The non-exhaustive list of buffering agents provided in Phillips I does not even suggest the specific combination of sodium carbonate and sodium bicarbonate together, let alone provided specifically in an equimolar ratio. There simply is nothing in Phillips I that discloses or suggests to a skilled artisan to specifically select a combination of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA

metal in an equimolar ratio out of all the possible general buffer combinations disclosed in Phillips I.

The Examiner goes on to state that

Applicant's argument that 'Phillips I does not disclose an equimolar ratio of a carbonate salt and a bicarbonate salt is presently claimed' is not persuasive since Applicants have not demonstrated any superior results attributable to the claims 'equimolar ratio' amount. The prior art vividly recognizes and teaches similar proton pump inhibiting formulations comprising the incorporation of suitable carriers and buffers to effectively treat acid-related gastrointestinal disorders. (See, Office Action, page 12).

Applicants respectfully disagree. As Applicants have previously argued, it is known in the art that sodium bicarbonate produces gas while neutralizing stomach acids. The formation of this gas causes distension of the stomach which results in a bloated feeling, belching and flatulence. Also, it is also known in the art that sodium bicarbonate ingestion can cause the spontaneous rupture of the stomach (see Applicant's discussion or supporting art in Applicant's response filed August 29, 2006).

Throughout the specification, the superior results specifically attributable to the equimolar ratio of sodium carbonate and sodium bicarbonate (hereinafter referred to as "carbicarb") are discussed and provided for, namely, the reduction in the comparative amounts of gas, including CO<sub>2</sub> gas, that is produced. This reduction in gas reduces the distension of the stomach, belching and flatulence experienced by patients who take the compositions solely containing sodium bicarbonate (such as those compositions disclosed in Phillips I and Phillips II). In addition, patients ingesting the compositions of the present invention may have a lower risk of stomach rupture when compared to patients who ingest compositions containing solely sodium bicarbonate.

As demonstrated by the Examples provided in the present invention, Applicants demonstrated that claimed equimolar ratio has an unexpected significant advantage over the prior art buffering agents. As discussed in the *Manual of Patent Examining Procedure*, Section 2144.05 III (8<sup>th</sup> Edition, Latest Revision August 2005), citing *In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990):

The last is replete with cases in which the difference between the claimed invention and the prior art is some range or other variable within the claims ...[I]n such a situation, the applicant must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range.

As the Examiner has continued to suggest, the Applicant must show that the particular range is critical. Accordingly, Applicants believe that they have demonstrated that the particular range (i.e., an equimolar ratio of bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal) is critical, since the use of this ratio results in a marked improvement relative to the prior art range. As discussed in the *Manual of Patent Examining Procedure*, Section 716.02 (8<sup>th</sup> Edition, Latest Revision August 2005), In *In re Weymouth*, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974), the court held that unexpected results for a claimed range as compared with the range disclosed in the prior art had been shown by a demonstration of "a marked improvement, over the results achieved under other ratios, as to be classified as a difference in kind, rather than one of degree." There simply is no teaching or suggestion anywhere in Phillips I that an equimolar ratio works better than other possible buffer combinations. Furthermore, the kind of improvement includes the prevention of stomach rupture and other gas related maladies. It was, therefore, not obvious for a skilled artisan to arrive at the conclusion that the equimolar ratio is indeed important. Accordingly, Applicants have satisfied the above discussed test.

b) Rejection over Phillips II in view of Phillips I.

The Examiner states that Phillips II teaches a method for treating gastric acid disorders by administering to a patient a single dose of a pharmaceutical composition including an aqueous solution/suspension of proton pump inhibitors in a pharmaceutically accessible carrier wherein the carrier comprises a bicarbonate salt of a Group IA metal. (See, Office Action, page 5). According to the Examiner, Phillips II also teaches a pharmaceutical composition which includes omeprazole or other substituted benzimidazoles and derivatives thereof in a pharmaceutically acceptable carrier wherein the carrier comprises a bicarbonate

salt of a Group IA metal. The Examiner further states that Phillips II teaches a method for treating gastric acid disorders wherein the Group IA metal is sodium and potassium.

According to the Examiner, the pharmaceutically acceptable carrier taught by Phillips II includes the bicarbonate salt of the Group IA metal and can be prepared by mixing the bicarbonate salt of the Group IA metal, preferably, sodium bicarbonate, with water. The Examiner states that the concentration of the bicarbonate salt generally ranges from approximately 5.0% to about 60.0%. The preferred salt is sodium bicarbonate and its preferred concentration in the solution is about 8.4%. (See, Office Action, page 7).

The Examiner acknowledges that Phillips II does not explicitly teach the equimolar ratio of bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Similarly, Phillips II does not teach an equimolar ratio of sodium bicarbonate and sodium carbonate. Nevertheless, the Examiner raises the argument which is essentially identical to the Examiner's argument in the §103(a) rejection over Phillips I, namely, that Applicants have not demonstrated any unusual/unexpected results that accrue from the instant equimolar ratios. (See, Office Action, page 7). According to the Examiner, it is obvious to a skilled artisan to arrive at suitable ratios and/or amounts through routine or manipulative experimentation. The Examiner states that the prior art recognizes that need to administer lower amounts of bicarbonate to avoid adverse effects. The Examiner further acknowledges that Phillips II does not teach a carbonate salt of the Group IA metal. However, the Examiner deems it obvious to a skilled artisan to include the carbonate salt of the Group IA metal of Phillips I with the teachings of Phillips II because Phillips I teaches buffering agents comprising both carbonates and bicarbonates of Group IA metals and teaches that the buffering agents function by elevating the stomach pH to achieve adequate bioavailability of the drug.

Applicants respectfully disagree. As discussed previously herein, Phillips I does not teach the equimolar ratio of a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. While Phillips I disclosed a broad mixture of possible buffering agents, there is no teaching or suggestion to use the equimolar mixture, specifically, carbicarb. Phillips II does not cure the deficiency of Phillips I since, as the Examiner acknowledges, Phillips II does not teach a carbonate salt of the Group IA metal at all. On the contrary,

Phillips II expressly states that in the preferred embodiment, omeprazole is mixed with a sodium bicarbonate solution to achieve a desired final omeprazole concentration. (See, Phillips II, column 7, lines 64-67). In fact, Phillips II is directed to a method of treating gastrointestinal conditions by administering omeprazole in a carrier with a bicarbonate salt of a Group IA metal, wherein the administration step consists of a single dosage. Therefore, a skilled artisan would not be motivated to replace the bicarbonate salt of a Group IA metal with an equimolar mixture of carbonate and bicarbonate. Phillips II allegedly works for its intended purpose, therefore there is no incentive for a skilled artisan to combine it with Phillips I to achieve the same purpose.

Therefore, contrary to the Examiner's argument, a skilled artisan would not have been motivated to include the carbonate salt of the Group IA metal of Phillips I with the teachings of Phillips II which teaches bicarbonate salts of the Group IA metal, among many other possible buffering agents. Even if one were to combine Phillips I and Phillips II, the resulting formulation would still not comprise an equimolar ratio of bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal. Therefore, Applicants respectfully submit that the rejections of claim 1-7, 9-21 and 23-33 under 35 U.S.C. §103 are improper and should be withdrawn.

## CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Section 103. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account no. 04-2223.

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